REMARKS

Status of the Claims and Amendment

Claim 2 has been amended. Claims 2, 4, 5, 9, 13, 16-19, 23, 28-30 and 32-35 are all the claims pending in this application. Claims 16-19, 23, 28-30 and 32-35 are withdrawn from consideration as being directed to a non-elected invention. Claims 2, 4-5, 9 and 13 are rejected.

Claim 2 has been amended to further clarify that the claimed oligonucleotide fragment is "at least 30 nucleotides in length" Support for the amendment to claim 2 may be found throughout the as-filed specification, for instance, at page 7.

The specification has also been amended at Table 1a, page 128, and pages 277-278 to correct for typographical and/or clerical errors. Table 3 has also been restored to its original appearance as shown in the as-filed specification.

No new matter is added.

Withdrawn Rejections and Objections

Applicants thank the Examiner for withdrawing the rejection of claims 2, 4, 9, and 13 under 35 U.S.C. § 102(b) as being anticipated by Ahr et al. (Journal of Pathology, 195: 312-320 (2001)).

In addition, Applicants thank the Examiner for withdrawing the objection to the Sequence Listing.

Information Disclosure Statement

Applicants thank the Examiner for returning a signed and initialed copy of the PTO Form SB/08 submitted with the Information Disclosure Statement filed July 6, 2009.

Response to Objections to the Specification

At pages 3 to 6 of the Office Action, the amendments to the specification filed October 3, 2008 and July 6, 2009 are objected to under 35 U.S.C. 132(a) because the amendment allegedly introduces new matter into the disclosure.

In response to Applicants' response and amendments to the specification, the Examiner appears to assert that because the amended pages in the International Patent Examination Report (IPER) filed May 19, 2005 were not entered by the International Search Authority, the amendments to the specification on July 6, 2009 and October 3, 2008 are maintained as constituting new matter, and does not support the amendments to the specification that have been submitted. Accordingly, the Examiner asserts that the amendments to the specification are inconsistent with the Sequence Listing filed May 1, 2006.

The Examiner appears to maintain the objection for the same reasons set forth in the previous Office Action. That is, the Examiner asserts that numerous SEQ ID NOs associated with each clone ID have been changed so that the clone ID of the specification now corresponds to different SEQ ID NOs. Specifically, the Office Action asserts that clone ID I-24 is listed in Table 1a of the specification filed October 3, 2008, as SEQ ID NO:11 and having 373[1] nucleotides, and as SEQ ID NO: 308 and having 373 nucleotides in the original specification filed May 19, 2005. However, the Examiner asserts that SEQ ID NO:11 (recited in the specification filed October 3, 2008) and SEQ ID NO:308 (recited in the original as-filed

[1] The Office Action at page 3, last paragraph states "371 nucleotides", but Applicants believe this is a typographical error as the Examiner later states that clone I-24 in the specification filed May 19, 2005 "also has 373 nucleotides."

specification) have different sequences. The same is asserted to be true for clone ID V-61 which is listed as SEQ ID NO: 308 in the specification filed October 3, 2008, and as SEQ ID NO: 721 in the original as-filed specification. In view of the above, the Examiner asserts that the amendment is not supported by the original disclosure.

In addition, on page 4, 2nd to last full paragraph of the Office Action, the Examiner points out some minor discrepancies in the number of nucleotides recited in the amended specification filed July 6, 2009 and the Substitute Sequence Listing for certain sequences, such as SEQ ID NO: 399 (recites 156 nucleotides in the amended specification but 155 in the Substitute Sequence Listing). Similarly, SEQ ID NOs: 36, 500, 499, 270, 337, and 388 are asserted for the same discrepancies between the number of nucleotides recited in the amended specification of July 6, 2009 and the Substitute Sequence Listing.

Furthermore, at pages 5 to 6 of the Office Action the Examiner asserts that Tables 1a, 2b, 3, 4a, 4b and 9 have deleted reference to a number of clones and/or have changed the SEQ ID NOs associated with each clone ID. The Examiner asserts that because the deletion of clone ID NOs and changes in SEQ ID NOs are neither an obvious error nor an obvious correction, the amendments constitute new matter. Further, the Examiner appears to assert that the deletion of certain clone IDs indicated as informative for disease diagnosis in the specification of May 19, 2005, changes the scope of the disclosure.

In response, and as discussed during the telephone conversation with the Examiner on January 26, 2010 (see Statement of Substance of the Interview), Applicants submit herewith sequence alignments performed by BLAST to demonstrate that the sequences in the Substitute Sequence Listing of October 3, 2008 (which are consistent with the Substitute Sequence Listing

of May 1, 2006) and the sequences in the "PCT application"[2] referenced by the Examiner in the Office Action (which is the as-filed specification of May 19, 2005) are the identical and the same.

Specifically, Applicants provide a sequence alignment to show that the sequences identified as SEQ ID NOs:1 to 498 and 500-501 in the Substitute Specification Listing filed October 3, 2008 and the sequences in as-filed specification of May 19, 2005 are the same. The Office Action is respectfully requested to note that the sequence identified as SEQ ID NO:499 in the Substitute Specification filed October 3, 2008 has been amended in the present Amendment to correct obvious typographical errors in the sequence that was unintentionally introduced at that time. Support for the amendment of SEQ ID NO:499 in the Substitute Specification filed October 3, 2008 may be found in the as-filed specification of May 19, 2005 (see SEQ ID:77) and the Substitute Sequence Listing filed May 1, 2006 (see SEQ ID NO:501). Further, "SEQ ID NO:499" has also been renumbered in the present Amendment to "SEQ ID NO:501", to be consistent with the Substitute Sequence Listing filed May 1, 2006. Accordingly, the typographical errors with regard to "SEQ ID NO:499" (now "SEQ ID NO:501") would have been apparent to one of ordinary skill in the art, and correction of these errors so that the disclosure is consistent with the originally filed specification of May 19, 2005 and the Substitute

[2] As the Examiner may recall, in the Amendment filed October 3, 2008, Applicants noted that a Sequence Listing was filed May 1, 2006 containing all the sequences disclosed in the original specification. The Sequence ID numbers listed in the original specification were not in consecutive order, starting at 93 and ending at 1495 (with many numbers missing in between). Additionally, Sequence IDs G6, 61, 490, 892 and 77 appeared at the end of the otherwise numerically increasing list. Subsequently a Sequence Listing was filed on May 1, 2006 in which the sequences were presented in a consecutive list of 501 sequences, but the sequences in the specification were inadvertently not amended at the same time to correspond to the list of 501 sequences. The Substitute Specification filed October 3, 2008 was merely provided to remedy this matter so that the original sequences disclosed correspond to the SEQ ID NOs in the Sequence Listing of May 1, 2006.

Sequence Listing of May 1, 2006, do not constitute new matter. In this respect, Applicants also provide a sequence alignment performed by BLAST to show the alignment for "SEQ ID NO:499" as an alignment between "SEQ ID NO:501" from the Substitute Sequence Listing filed May 1, 2006 and SEQ ID:77 of the as-filed specification of May 19, 2005 (which is the "PCT application" referenced by the Examiner in the Office Action). Thus, the sequence alignments performed by BLAST submitted herewith show that all the sequences of the Substitute Specification filed October 3, 2008 and the as-filed specification of May 19, 2005 are identical and the same sequences.

With regard to the minor discrepancies asserted on page 4 of the Office Action between the sequences disclosed in the PCT application (i.e., the as-filed specification) and the Substitute Specification of October 3, 2008, Applicants note that the minor discrepancies would have been understood and recognized by one of ordinary skill in the art to be typographical and/or clerical errors based upon the sequences disclosed in the as-filed specification of May 19, 2005 and the Substitute Sequence Listing filed May 1, 2006. Specifically, Table 1a has been amended to correct these errors so that the number of nucleotides for: (1) SEQ ID NO:399 recites "155" instead of "156", (2) SEQ ID NO:36 recites "527" instead of "528", (3) SEQ ID NO:270 recites "591" instead of "691", and (4) SEQ ID NO:377 recites "501" instead of "601". In addition, the Table 1a has been amended a clerical error so that SEQ ID NO:388 recites "561" nucleotides instead of a "-".

With regard to the Examiner's assertion on page 3 of the Office Action that "SEQ ID NO 11 and SEQ ID NO 308 although having the same number of nucleotides have different sequences". Applicants note that the sequence alignment submitted herewith shows that the

sequence identified as "SEQ ID NO:11" in the Substitute Specification of October 3, 2008 and "SEQ ID: 308" of the as-filed specification of May 19, 2005 are identical.

With regard to the Examiner's assertion on page 3 of the Office Action that the Substitute Specification of October 3, 2008 "lists clone ID V-61 as SEQ ID NO 308 and the specification of May 19, 2005 lists V-61 as SEQ ID NO 721", Applicants note that the amendment made in the Substitute Specification is correct. As shown on page 88 of the marked-up specification submitted October 3, 2008, clone ID V-61 in Table 1b was amended so that the sequence referenced as "SEQ ID 721" in the as-filed specification of May 19, 2005 was renumbered as "SEQ ID NO:308" to be consistent with the Substitute Sequence Listing of May 1, 2006. Also, as shown in the sequence alignment submitted, the sequence identified as "SEQ ID NO:308" in the Substitute Specification of October 3, 2008 and "SEQ ID: 721" of the as-filed specification of May 19, 2005 are identical.

Furthermore, with regard to the Examiner's assertions that the deletion of clones referenced in Tables 1a, 2b, 3, 4a, 4b and 9 and/or the change of SEQ ID NOs associated with each clone ID constitute new matter, Applicants note that as previously addressed, the Tables were amended to remove clones with sequences indicated as "missing" or did not reference a sequence. However, because no actual sequences were provided in the original specification filed May 19, 2005 in connection with these clones, these sequences are technically not missing insofar as there were no actual sequences provided in the original disclosure. Also, as shown in the sequence alignment submitted herewith, the change of SEQ ID NOs is consistent with the Substitute Sequence filed May 1, 2006 and the sequences disclosed in the as-filed specification of May 19, 2005.

Thus, as shown by the sequence alignment submitted herewith, the sequences of the Substitute Specification filed October 3, 2008 (which is consistent with the Substitute Sequence Listing filed May 1, 2006) and the sequences of the as-filed specification of May 19, 2005 are the same. Correction of the above typographical errors in the present Amendment do not constitute new matter.

Withdrawal of the grounds of objection is respectfully requested.

Response to Rejection Under 35 U.S.C. § 112

Claims 2, 4-5, 9 and 13 remain rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement requirement. The rejection appears to be maintained for the same reasons set forth in the previous Office Action. That is, the Examiner appears to assert that (1) the specification does not disclose the claimed combination of probes that are informative for the diagnosis of disease states, and (2) the claims are not limited to sequences disclosed, but also encompass fragments and fragments with a certain percent identity so that it would be unpredictable to diagnose cancer based on these claimed fragments.

Specifically, it appears the claims are asserted to not be enabled due to the new matter issues discussed above for the specification. In this respect, with regard to (1), the Examiner's position appears to be that the amendments to the specification have resulted in inconsistencies in the disclosure and thus the unpredictability of the claimed invention.

With regard to (2), the Examiner asserts that although one of the previous issues involved was the interpretation that the claims did not did not necessarily require the replaced probe be from the claimed sequences being replaced, the other issue concerned the use of any fragment of the claimed SEQ ID NO that is at least 20 nucleotides of the SEQ ID NO being replaced, or at least 20 nucleotides and completely complementary to the sequence being replaced, or at least

80% identity to the sequence being replaced or a fragment thereof. The Examiner appears to assert that Applicants' arguments of July 6, 2009, are not persuasive because the specification provides no indication that every or any 20 base fragment of the recited SEQ ID NOs allow detection as the full length sequences taught by the specification to be indicative of differential expression patterns, so that detection by the claimed fragments would be unpredictable.

Thus, the Examiner appears to conclude that based upon the discrepancies in the disclosure, one of ordinary skill in the art would not know which probes are required or the number of probes that are informative. The Examiner asserts that claims requiring the entire sequence of the probes are enabled if the new matter issues can be overcome.

In response, and solely to advance prosecution of the present application, claim 2 has been amended to further clarify that the fragments are "at least 30 nucleotides in length".

Furthermore, as discussed in detail above, and suggested by the Examiner during the telephone call of January 26, 2010 (see Statement of Substance of the Interview submitted herewith), Applicants submit herewith sequence alignments to show that the sequences in the Substitute Specification filed October 3, 2008 and the sequences in the as-filed specification of May 1, 29005 are the same. Applicants note that this sequence alignment supports the previously presented arguments and Declaration by Praveen Sharma to demonstrate that the specification enables one of ordinary skill in the art to make and use the claimed invention.

Reconsideration and withdrawal of the rejection under 35 U.S.C. §112, first paragraph, is respectfully requested.

Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the

Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,

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